

1-Octanol/Water Partition Coefficient (K_{ow}) and pK_a for Ionisable Pesticides Measured by a pH-Metric Method

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Abstract: pK_a values for a wide range of commonly used ionisable pesticides, together with the $\log K_{ow}$ values of the most lipophilic form of each, have been measured using pH-metric techniques. Examples of acids, bases and multiprotic compounds from the major classes of herbicides, and a number of insecticides and fungicides that contain ionisable groups, are included. The pK_a and $\log K_{ow}$ values so obtained were generally in good agreement with values taken from the literature that were measured by other methods.

The lower limit of $\log K_{ow}$ that could be measured by the pH-metric method lay below the -0.97 obtained for amitrole, but the method could not be applied to glyphosate for which shake-flask measurements indicated $\log K_{ow}$ below -3 . The highest $\log K_{ow}$ obtained in this study was 5.12 for pentachlorophenol.

The pH-metric technique offers a rapid and convenient method to determine pK_a and $\log K_{ow}$ for ionisable compounds, especially when utilising an automatic titration system linked to a dedicated computer.

Key words: $\log K_{ow}$, pK_a , pesticides, pH-metric, glyphosate

1 INTRODUCTION

The fate and behaviour of pesticides and their metabolites in the environment are largely dependent on the physicochemical properties of the compounds. In particular, the lipophilicity of a compound, usually expressed as its partition coefficient between 1-octanol and water (K_{ow}), is the most important parameter determining uptake and translocation in plants and, usually, also sorption to soils and hence the potential to leach from them. Biological activity is also often strongly influenced by $\log K_{ow}$, although other parameters are normally involved as well. For ionisable pesticides, their pK_a values determine the degree of ionisation in water at the pH of the soil or biological system, and this in turn determines their effective lipophilicity. Accurate values for pK_a and $\log K_{ow}$ are therefore necessary to model pesticide behaviour or to carry out QSAR studies with series of active compounds. The measurement of $\log K_{ow}$ for ionisable compounds, especially multiprotic and zwitterionic ones, presents problems

using conventional methods. This is also true for the measurement of pK_a values for compounds that are sparingly soluble in water.

Ionisable compounds normally have their highest $\log K_{ow}$ value when non-ionised; for monoprotic carboxylic acids, the $\log K_{ow}$ of the anion is typically 3–3.5 units lower than that of the acid.¹ For zwitterionic compounds, such as glyphosate, there may not be any pH at which the compound is not substantially ionised. Thus, for the determination of $\log K_{ow}$ by the conventional methods of shake-flask,² HPLC³ or centrifugal partition chromatography,⁴ it is essential, even for monoprotic substances, that the pK_a be known or measured beforehand and that the $\log K_{ow}$ measurement be made with the aqueous phase buffered to a suitable pH. Separate experiments at different pH values are then needed to determine which species is the most lipophilic. In the present study, this approach is illustrated by the measurement of the $\log K_{ow}$ of glyphosate at several pH values using the shake-flask method.

An alternative method to those mentioned above is available for ionisable compounds in which the pK_a of the compound is measured potentiometrically by acid–

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base titration in aqueous solution.^{5,6} An appropriate amount of 1-octanol can then be added to the solution and the compound allowed to partition between the two phases; the apparent pK_a (p_oK_a) is then measured as before. The resulting shift in pK_a (i.e. $pK_a - p_oK_a$) is related to the $\log K_{ow}$ of the compound, and computation using non-linear least squares procedures can allow for sources of inaccuracy in the titration (e.g. errors in substance concentration, dissolved carbon dioxide, changing ionic strength) to give accurate values for $\log K_{ow}$ as well as pK_a .⁷

For compounds whose water solubility is too low ($<10^{-4}$ M) to determine the pK_a by potentiometric titration, the measurement may be carried out using mixtures of water and a miscible co-solvent. The apparent pK_a (p_sK_a) is measured in three or more different mixtures, and the aqueous pK_a is calculated by extrapolation to zero co-solvent using the Yasuda-Shedlovsky procedure which plots the sum of p_sK_a and \log [concentration of water in the mixture] against a function of the dielectric constant.⁸

Using these methods, the pK_a and $\log K_{ow}$ of the most lipophilic form for 30 ionisable pesticides have been determined and the results compared with those in the literature. Many literature references to these physicochemical properties cite values for both pK_a and $\log K_{ow}$ with no indication of the source or the method of measurement, and, furthermore, $\log K_{ow}$ values for ionisable pesticides often appear with no indication of the pH at which the determination was made. It is hoped that this study will go some way towards rectifying that situation.

2 EXPERIMENTAL

2.1 Chemicals

Pure samples of the pesticides used were gifts from the manufacturer, purchased from suppliers or in a few cases synthesised and characterised according to the published methods. [¹⁴C]Glyphosate was a gift from Monsanto Co.

2.2 pH-Metric method

All titrations were done using a PCA 101 (Sirius Analytical Instruments Ltd) automated titrator which incorporated a microcontroller and a dedicated computer. The latter was used for all calculations. All titrations were done at $25(\pm 1)^\circ\text{C}$ and at a mean ionic strength of approximately 0.16 M, achieved by using 0.15 M potassium chloride solution to make up aqueous or water/methanol solutions (titration increases the initial ionic strength of 0.15 M to about 0.17 M). 1-Octanol used in the experiments was pre-saturated with aqueous 0.15 M potassium chloride solution.

2.2.1 Blank titration

Before each titration or series of titrations, the semi-micro pH electrode was standardised. Aqueous potassium chloride solution (0.15 M, 20 ml) was placed in the titration vessel and sufficient 0.5 M hydrochloric acid added automatically to adjust the pH to 1.8. This was then titrated up to pH 12.2 with standardised 0.5 M potassium hydroxide.

2.2.2 $pK_a/\log K_{ow}$ measurement for water-soluble compounds

A sufficient quantity of the pesticide to give a concentration of around 10^{-3} M when dissolved in 0.15 M aqueous potassium chloride (20 ml) was weighed into the titration vessel. The instrument was programmed to add the ionic-strength adjusted water, adjust the pH to the starting pH of the titration by addition of acid or base and to titrate with base or acid until a specified pH was reached. The starting and final pH were chosen to be at least two pH units either side of the expected pK_a .

In some cases the instrument was also set to add, when the first titration was complete, an aliquot of 1-octanol, whose chosen volume depended on the expected $\log K_{ow}$, and then to repeat the titration on the same sample, either in the reverse direction or in the same direction. In other cases, particularly for relatively polar compounds where larger ratios of octanol to water were needed, a second titration in the presence of 1-octanol on a fresh sample of compound was done. All experiments were replicated at least three times.

2.2.3 $pK_a/\log K_{ow}$ for compounds of low water solubility ($<10^{-4}$ M)

A similar amount of substance to that used in Section 2.2.2. was weighed into the titration vessel and the instrument programmed to add a certain volume of aqueous 0.75 M potassium chloride + methanol (1 + 4 by volume) followed by the required amount of ionic-strength-adjusted water to bring the total volume to 20 ml. The titration was then done as previously. For each pK_a determination, it was necessary to repeat this procedure for at least three different ratios of methanol to water; reported pK_a values are means of three such determinations.

Having determined the pK_a in this way, $\log K_{ow}$ was measured in a separate experiment by first dissolving the material in the 1-octanol and then adding automatically the appropriate amount of ionic-strength-adjusted water before doing the titration as above.

2.2.4 Calculation of results

Full details of the mathematics involved in refining values of pK_a and $\log K_{ow}$ from the raw data are given elsewhere.^{7,8}

Inputs necessary when programming the instrument to perform titrations are weight of substance, molecular weight, type of experiment (pK_a , $\log K_{ow}$ or combined $pK_a/\log K_{ow}$), direction of titration and ratio of 1-

octanol to water or ratio of methanol to water where appropriate. Upon completion of the titration, it is necessary to enter an ionisation model for the compound, including an indication of the charge status of the form of compound used (e.g. hydrochloride, sodium salt(s)).

Initially a difference curve is exhibited which is a plot of the number of bound protons in each molecule of the substance against pH and represents the sample titration curve minus the blank titration curve.⁶ An example of difference curves, with and without 1-octanol, for the herbicide imazapyr is shown in Fig. 1. The pH values at which the curves intercept the half-integral numbers of bound protons per molecule give first approximations of pK_a and p_oK_a (or p_sK_a if it is a methanol/water titration). These values are then refined by a generalised non-linear least-squares procedure which takes other variable factors into account. Log K_{ow} values are calculated from the difference between the p_oK_a and the pK_a , both of which values have already been determined for a combined experiment; alternatively, to determine log K_{ow} from a single titration in the presence of 1-octanol, the pK_a value must be known and entered for the computation. A similar procedure to that used to refine the pK_a values then gives an accurate value for the log K_{ow} . For multiprotic substances, the shapes of the two different curves, with and without 1-octanol, are used to indicate which species partitions the most into the organic phase.⁹

For titrations done in mixtures of water and methanol, the Yasuda–Shedlovsky procedure is used to calculate aqueous pK_a from three or more p_sK_a values (measured pK_a in water/methanol) by plotting $p_sK_a + \log [H_2O]$ against the reciprocal of the dielectric constant (ξ) for the mixture and then extrapolating to zero methanol (i.e. ξ 78.3).⁸

2.3 Log K_{ow} of glyphosate by shake-flask method

Four aqueous buffer solutions were made up as follows:
A. 0.2 M potassium chloride (25 ml) + 0.2 M hydrochloric acid (12 ml) + water (63 ml); pH 1.77

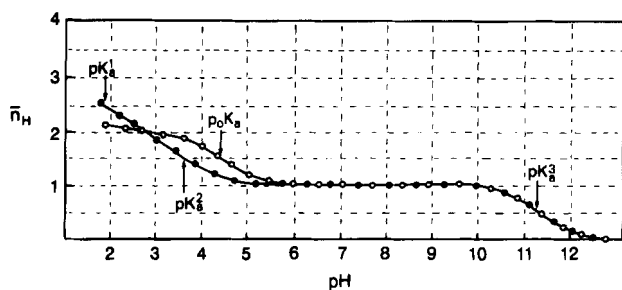


Fig. 1. Difference curves for imazapyr titrated in the (●) absence and (○) presence of 1-octanol (with a volume ratio of 1-octanol : water of 4). \bar{n}_H is the average number of ionisable protons associated with each molecule of substance. Superscripts 1, 2 and 3 identify the three separate ionisations of imazapyr.

- B. 0.2 M sodium acetate (26.5 ml) + 0.2 M acetic acid (73.5 ml); pH 4.61
- C. 0.2 M disodium hydrogen phosphate (24.5 ml) + 0.2 M sodium dihydrogen phosphate (25.5 ml) + water (50 ml); pH 6.86
- D. 0.025 M sodium borate (50 ml) + 0.1 M hydrochloric acid (7.1 ml) + water (42.9 ml); pH 9.00.

Each buffer solution (20 ml) was shaken with 1-octanol (50 ml) and the layers separated by centrifugation for 15 min at 1500g. Unlabelled glyphosate (5 mg) was added to each 1-octanol-saturated buffer (15 ml) to give an approximately 2 mM solution. To a sample (2 ml) of each buffer was added 1-octanol-saturated water (0.5 ml) and the pH measured. These solutions were used for the determinations.

An aqueous stock solution of [^{14}C]glyphosate (1 ml; approx. 1 mM; 74 kBq μmol^{-1}) was shaken well with water-saturated 1-octanol (2×5 ml) and the layers separated following centrifugation for 15 min at 1500g. The 1-octanol washings were discarded and replicate aliquots ($3 \times 50 \mu\text{l}$) of the washed stock solution removed and radioactivity measured by liquid scintillation counting.

For each pH point, three replicate experiments to measure log K_{ow} were made together with a blank containing no radioactivity. For each experiment, purified stock solution of [^{14}C]glyphosate ($50 \mu\text{l}$; 0.97 mM; 74 kBq μmol^{-1}) was added to the appropriate 1-octanol-saturated buffered solution of unlabelled glyphosate (200 μl) and buffer-saturated 1-octanol (10 ml). The phases were mixed well by vortexing for 2 min and then left to stand in a stoppered tube overnight. The mixture was centrifuged for 15 min at 1500g and radioactivity in the organic layer measured by counting aliquots (3×0.5 ml). K_{ow} was calculated as the ratio of the concentration in the 1-octanol phase to that in the water phase.

3 RESULTS AND DISCUSSION

pK_a and log K_{ow} values measured by the pH-metric technique are shown in Table 1. Bearing in mind that the pK_a values measured by the pH-metric method have been adjusted to zero ionic strength while those taken from the literature have not been adjusted and the ionic strength was usually not reported, the agreement is extremely good for almost all of the pesticides used. Furthermore the temperature of measurement for the published values is variable and not always quoted. In cases where there is a range of published pK_a values, as for mecoprop and bentazone, the pH-metric value falls within that range. Values of aqueous pK_a obtained by measurement in methanol/water mixtures with extrapolation to zero methanol in general agree extremely well with the published values.

TABLE 1
Comparison of pK_a and $\log K_{ow}$ Values Measured by pH-Metric Method with Published Values

Pesticide ^a	pK_a^b		$\log K_{ow}^c$	
	Measured	Published ^d	Measured	Published ^d
Amitrole (h)	10.72 (± 0.02) 4.19 (± 0.02)	11.1, 4.0; ¹⁰ 4.17; ¹¹ 4.2 ¹²	-0.97 (± 0.03)	<0; ¹⁰ -0.87; ¹³ -0.85 ¹⁴
Bentazone (h)	2.91 (± 0.05)	4.0; ¹² 3.5; ¹³ 3.3; ¹⁵ 2.7; ¹⁶ 3.45 ¹⁷	2.83 (± 0.05)	0.77 (pH 5); ¹⁵ 1.38 (pH 2) ¹⁷
Chlorsulfuron (h)	3.63 (± 0.02) ^e	3.6; ¹¹ 3.6; ¹² 3.6; ¹⁵ 3.6; ¹⁸ 3.6; ¹⁹ 3.8 ²⁰	1.79 (± 0.06)	-1.0 (pH 7); ¹⁵ 0.11 (pH 5.4); ¹⁸ 2.2; ¹⁹ 1.54 ²⁰
Clopyralid (h)	2.32 (± 0.07)	2.3; ¹¹ 2.3; ¹² 2.33; ¹³ 2.3; ¹⁵ 2.3 ¹⁸	1.07 (± 0.03)	1.5; ¹³ -1.8 (pH 5); ¹⁵ -2.74 (pH 5.4) ¹⁸
Ethirimol (f)	11.06 (± 0.01) 5.04 (± 0.02)	10.87, 4.85 ¹⁰	2.22 (± 0.01)	2.25; ¹⁰ 2.3 (pH 7); ¹⁵ 2.2; ²¹ 2.2 (pH 7) ²²
Fenpropimorph (f)	7.34 (± 0.05) ^e	6.98 ¹⁵	4.93 (± 0.07)	4.4 (pH 9); ¹⁵ 5.87 (calc) ²³
Flamprop (h)	3.73 (± 0.07) ^e	3.7; ¹ 3.7; ²⁰ 3.46 ²³	3.09 (± 0.01)	2.9; ¹ 2.9; ²⁰ 2.90 ²³
Fluazifop (h)	3.22 (± 0.03) ^e	3.0 ¹²	3.18 (± 0.07)	(butyl ester 4.5) ¹⁵
Fomesafen (h)	3.09 (± 0.15)	2.7; ¹¹ 3.0; ¹² 2.7 ¹⁵	3.00 (± 0.01)	2.9; ¹⁵ 2.9 ²¹
Glyphosate (h)	10.98 (± 0.03) 5.96 (± 0.02) 2.29 (± 0.03) 0.78 (± 0.21)	10.9, 5.86, 2.3; ¹¹ 10.9, 5.9, 2.3; ¹² 10.2, 5.6, 2.3, <2 ²⁴	Not measured	-4.0 (pH 7) ²²
Imazapyr (h)	11.34 (± 0.04) 3.64 (± 0.03) 1.81 (± 0.15)	3.6, 1.9; ¹¹ 10.5, 1.8; ¹² 3.6, 1.9; ¹⁵ 3.55, 1.65 ²⁵	0.22 (± 0.04) (pH 2.7)	0.16; ¹³ 0.11; ¹⁵ 0.24 (pH 2.6); ²⁵ -2.40 (pH 7), -0.93 (pH 4) ²⁶
Imazaquin (h)	11.14 (± 0.03) ^e 3.74 (± 0.05) ^e 2.04 (± 0.15) ^e	3.8; ¹¹ 10.2, 3.2; ¹² 3.8; ¹⁵ 3.9; ²³ 3.45, 2.00 ²⁵	1.86 (± 0.06) (pH 2.9)	0.34; ¹⁵ 0.64 (pH 4); ²³ 1.81 (pH 2.7); ²⁵ 0.89 (pH 4) ²⁶
Imazethapyr (h)	3.91 (± 0.05) 2.03 (± 0.06)	3.9, 2.1; ¹¹ 10.0, 3.9; ¹² 3.9, 2.1; ¹⁵ 3.9; ²³ 3.7, 1.75 ²⁵	q1.21 (± 0.04) (pH 2.9)	1.5 (pH 7); ¹⁵ 1.09 (pH 2.7); ²⁵ 0.14 (pH 4), -1.77 (pH 7) ²⁶
Imidacloprid (i)	11.12 (± 0.11) 1.56 (± 0.12)	None found	0.33 (± 0.42)	0.57 ¹⁵
Ioxynil (h)	4.08 (± 0.04) ^e	4.0; ¹² 4.06; ¹³ 3.96; ¹⁵ 3.9 ²⁷	3.43 (± 0.01)	3.1; ¹³ 3.8 ²⁷
Maleic hydrazide (pgr)	5.79 (± 0.01)	5.67; ¹⁰ 5.65; ¹¹ 5.65; ¹³ 5.62; ¹⁵ 5.65; ¹⁹ 5.65; ²⁸ 5.67 ²⁹	-0.56 (± 0.02)	-0.63; ¹ 0.84; ¹⁰ -0.87; ¹³ -1.96 (pH 7); ¹⁵ -0.84; ¹⁹ -0.9; ²² -0.84 ²⁹
Mecoprop (h)	3.21 (± 0.04)	3.11; ¹¹ 3.78; ¹⁵ 3.38; ²³	3.21 (± 0.01)	3.1; ¹³ 0.1 (pH 7); ¹⁵ 2.99 ²³
Mefluidide (h)	4.79 (± 0.04) ^e	4.6 ¹⁵	2.02 (± 0.01)	None found
Metsulfuron-methyl (h)	3.64 (± 0.03)	3.3; ¹¹ 3.3; ¹² 3.3; ¹⁵ 3.3 ²³	1.58 (± 0.05)	-1.74 (pH 7); ¹⁵ 1.72 & 2.2 ²³
Nicotine (i)	8.18 (± 0.02) 3.09 (± 0.02)	7.84, 3.04; ¹⁵ 7.9 ³⁰	0.93 (± 0.12)	1.17 ³¹
Pentachlorophenol (f)	4.69 (± 0.02) ^e	4.71; ¹⁵ 4.7; ²⁷ 4.8 ³¹	5.12 (± 0.10)	5.1; ²⁷ 5.01; ³¹ 5.01 ³²
Pirimicarb (i)	4.54 (± 0.01)	None found	1.71 (± 0.05)	1.7 ¹⁵
Pirimiphos-methyl (i)	3.71 (± 0.12) ^e	None found	3.27 (± 0.19)	4.2; ¹⁵ 4.10; ²¹ 4.2 ³³
Propamocarb (f)	9.48 (± 0.01)	9.1; ¹¹ 9.1 ¹⁵	1.12 (± 0.09)	(hydrochloride -2.74) ¹⁵

TABLE 1. (continued)

Pesticide ^a	pK _a ^b		Log K _{ow} ^c	
	Measured	Published ^d	Measured	Published ^d
Quinmerac (h)	3.96 (±0.02)	4.31; ¹⁵	0.78 (±0.04)	−1.11 (pH 7), ¹⁵
Sethoxydim (h)	4.58 (±0.18) ^e	4.6; ¹² 4.62 ³⁴	4.38 (±0.03)	4.51 (pH 5), 1.65 (pH 7) ¹⁵
Thiabendazole (f)	4.64 (±0.01) ^e 1.87 (±0.06) ^e	4.7; ¹¹ 4.7 ¹²	1.94 (±0.02)	2.3; ²³ 2.47 (pH 6) ³⁵
Tralkoxydim (h)	4.98 (±0.05) ^e	4.3 ¹⁵	4.46 (±0.01)	2.1 ¹⁵
Triazamate acid (i)	3.49 (±0.02)	None found	1.62 (±0.02)	(ethyl ester 2.69) ¹⁵

^a Letter in parentheses indicates h-herbicide, f-fungicide, i-insecticide, pgr-plant growth regulator.

^b Measured pK_a values have been adjusted to zero ionic strength; ionic strength is not quoted for any of the published values.

^c Measured log K_{ow} is the maximum obtained and for all but the imidazolinone herbicides is that of the non-ionised compound. For the imidazolinone herbicides the pH at which log K_{ow} is maximum is given. Where possible the pH for literature values of log K_{ow} is given.

^d Methods of measurement are given in the reference for those values in italics; pK_a values separated by commas are for multiple ionisations, whilst semi-colons separate values from different sources.

^e Aqueous pK_a determined by extrapolation from three or more values of p_sK_a (measured pK_a in methanol/water mixtures) by Yasuda-Shedlovsky procedure.

The log K_{ow} of an ionisable compound varies with pH. It is therefore important when measuring log K_{ow} for such compounds to ensure, if possible, that the pH is such that essentially only one species is present. For monoprotic substances this is best done by measuring log K_{ow} at least three and preferably four pH units from the pK_a. For such compounds, it is almost always the non-charged species that is the most lipophilic. In cases such as that for zwitterionic compounds where it is not possible to determine the log K_{ow} of a single uncharged species, the maximum log K_{ow} found and the pH at which it occurs should be recorded. This is likely to be for the zwitterion itself but may not always be so, since ion-pair partitioning⁹ can play an important role for these instances.

Many of the references in the literature to log K_{ow} of ionisable pesticides do not make clear the degree of ionisation of the compound, and this omission makes it difficult to judge the accuracy of the value. This could explain the discrepancy in Table 1 between the measured and published value for tralkoxydim. In other cases where the determinations have been done at a range of pH values, presumably to reflect physiological or environmental pH ranges, they do not include the value for the uncharged species, which often makes comparison difficult, e.g. bentazone (Table 1). The pH-metric method used here always gives a value for the log K_{ow} of the most lipophilic species and the pH or range of pH values at which it occurs. For almost all of the pesticides in Table 1, the measured value is for the uncharged species but for the imidazolinone herbicides it is not known whether this is so and the pH at which the maximum log K_{ow} occurs is given.

For propamocarb, the published value for log K_{ow} is for the fully protonated species, in the form of the

hydrochloride, and for quinmerac the only published value found is for the anion. The value quoted in the literature for triazamate, which is the ethyl ester of the acid measured here, is approximately one unit higher than that for the acid. Given that the hydrophobic (π) constant³⁶ for the ethyl group is approximately 1, these results are in perfect agreement. The agreement is not so good for fluazifop where the only published value is for the butyl ester (log K_{ow} 4.5) and which, based on π values given by Hansch and Leo,³⁶ should have log K_{ow} approximately 2.1 units higher than the acid, i.e. this predicts a log K_{ow} of 2.4 for fluazifop acid, but the value measured by the pH-metric technique is 3.18; this measured value seems consistent with values obtained for similar compounds such as flumetop, and so the predicted value is likely to be in error. The largest discrepancy between published and measured values for log K_{ow} in Table 1 occurs for pirimiphos-methyl, for which there is no obvious explanation, although calculation from the log K_{ow} value of pirimicarb, using π constants, gives a value closer to the pH-metric measurement.

Log K_{ow} values for glyphosate could not be measured by the pH-metric method as described here, presumably because it is too polar at all pH values owing to its complex ionisation pattern. The only published value for glyphosate is −4.0 measured at pH 7 but there is no indication as to whether this is for the most lipophilic species. In an attempt to get a better idea of the maximum value, the log K_{ow} of [¹⁴C]glyphosate was measured by the alternative method of shake-flask at four different pH values, chosen to be roughly midway between the pK_a values for glyphosate. The results (Table 2) indicate that the highest value occurs for the species with a single negative charge on a phosphonate oxygen and a positive charge on the nitrogen, i.e. the

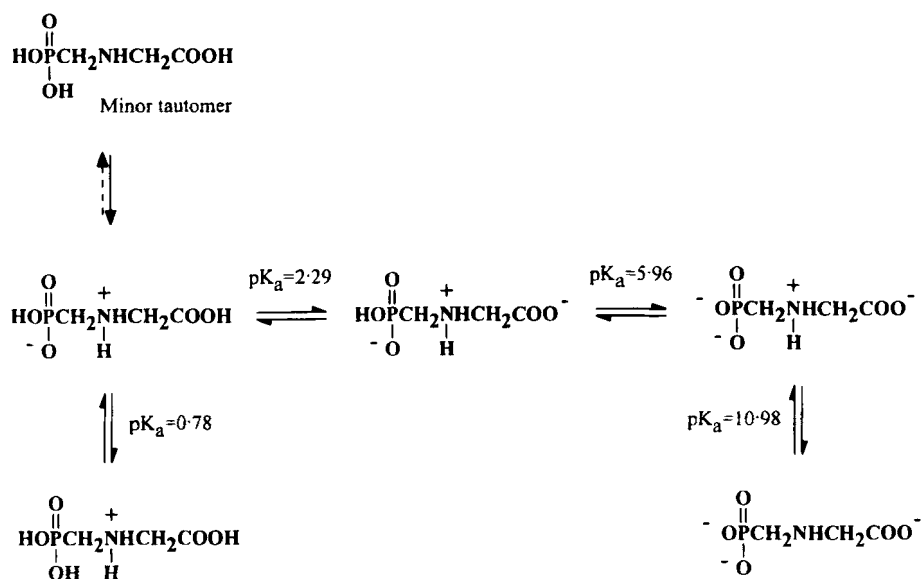


Fig. 2. Glyphosate and the major species present in its ionisations.

species present at pH values between the two lower pK_a values (Fig. 2). However, no measurement was made below the pK_a of 0.78 for the species with just a positive charge or above the pK_a of 10.98 for the trianion.

The $\log K_{ow}$ value for amitrole (Table 1) is -0.97 and was measured with no difficulty using the pH-metric method with a ratio of octanol to water of 3. The lower limits of measurement of $\log K_{ow}$ therefore lie somewhere between the values of -1 for amitrole and -3.4 for glyphosate. The upper limits of measurement were not adequately tested in this study, the highest $\log K_{ow}$ measured being 5.12 for pentachlorophenol, in good agreement with literature values. In a recent review,³⁷ the shake-flask method was recommended only for compounds of $\log K_{ow}$ -2.5 to 4.5 and HPLC for the range 0 to 6 . Another review³⁸ suggests a wider range of $\log K_{ow}$ of -5 to 5 , for the shake-flask method, and a range of -4 to 4 for the related stir-flask technique. The limits of the pH-metric method are thus similar to those for other methods.

Within the limits set out above, the pH-metric method of simultaneously measuring pK_a and $\log K_{ow}$ for ionisable compounds is extremely quick and convenient, particularly by using an automatic titration system coupled to a dedicated computer. The results

obtained in this study for 30 ionisable pesticides, in general, are in good agreement with values of pK_a and $\log K_{ow}$ measured by other methods and published in the literature.

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TABLE 2

Log K_{ow} Values for Glyphosate Measured by Shake-Flask Method at Four pH Values

pH	Mean log K_{ow}
1.77	$-3.39 (\pm 0.03)$
4.61	$-4.38 (\pm 0.05)$
6.86	$-4.85 (\pm 0.17)$
9.00	$-4.14 (\pm 0.03)$

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